Comparative Effectiveness Review Disposition of Comments Report

Research Review Title: *Treatments for Ankyloglossia and Ankyloglossia With Concomitant Lip-Tie*

Draft review available for public comment from October 28, 2014, to November 25, 2014.

Research Review Citation: Francis DO, Chinnadurai S, Morad A, Epstein RA, Kohanim S, Krishnaswami S, Sathe NA, McPheeters ML. Treatments for Ankyloglossia and Ankyloglossia With Concomitant Lip-Tie. Comparative Effectiveness Review No. 149. (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2012-0009-I.) AHRQ Publication No. 15-EHC011-EF. Rockville, MD: Agency for Healthcare Research and Quality. May 2015. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Comments to Research Review

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

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Commentator & Affiliation	Section	Comment	Response
Peer reviewer #1	Discussion / Conclusions	This area clearly states all of the major findings and limitations of the study that are very significant in this review because of the limited amount of studies. They also do a great job of identifying the gaps that indicate where future research is indicated and the need for a standardized approach to the identification and classification of ankyloglossia.	Thank you for your comment.
Peer reviewer #1	General Comment	Clarity and Usability: The report is well structured and adequately organized. The main points were presented well and understandable. However, the conclusions in this report are not yet ready to inform policy or practice decisions due to lack of evidence. It can only direct the field to future research and best practice development needs.	No change needed.
Peer reviewer #1	General Comments	This report will not have a direct effect on clinical practice at this time due to lack of significant evidence. However, it does highlight some gaps in knowledge that need to be addressed as a next step.	Thank you for your comment.
Peer reviewer #1	Introduction	The topic overview was adequately reviewed, and the target audience and population are clearly defined.	Thank you for your comment.
Peer reviewer #1	Methods	The study selection and review as well as the data extraction processes were clearly defined and justifiable given the use of independent reviews. The data synthesis elements of risk of bias and quality ratings were clearly defined as well. The process for rating the overall strength of evidence using two senior independent reviews was appropriate.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
Peer reviewer #1	Results	For the majority of the Key Questions the information presented is clearly described and appropriate. However, for KQ 3 and KQ 5 I believe there were some missing elements. The KQ 3 overview of the literature did not include a discussion of the quality ratings for the studies identified. I assume this was because it was determined that the evidence was not sufficient to assess the effects of intervention on social concerns as noted in the key points. However, the quality is noted in Table 12 so it would have been a good addition to the section to have a brief discussion on why the rate was given. The same question is for KQ 5. There is no discussion of the quality of studies that were reviewed.	The quality ratings are provided in the overview of KQ 3. Many of the harms papers were those included in the other questions, and quality is available for those. However, the expanded search included case reports, for which we assumed low quality given the high risk of bias inherent in the design.
Peer reviewer #2	Discussion/ Conclusion	Discussion/ Conclusion: I felt the description of the content and quality of existing research was very clear. The structure and fundamental questions are well defined. I think this will provide a needed platform for further discussion and direction of study.	Thank you for your comment.
Peer reviewer #2	General	General Comments: This report is very meaningful. We are seeing a great deal of conflict because of local lactation nurses that direct every child with lactation problems for fenulectomy. It's helpful for better definition of the problem, stress on need for better definition/study and the ef ignition of current evidence.	Thank you for your comment.
Peer reviewer #2	General	Clarity and Usability: I felt that the content was clear and well organized. It did seem a bit repetitive. This is my first review. My perception may just be the standard form that this type of paper must comply with in content.	Thank you for your comment. We have edited the report throughout to attempt to reduce repetition.
Peer reviewer #2	Introduction	Key questions are good. It might be helpful to explicitly separate the breastfeeding experience (ie pain and latch) vs a separate question of change in breastfeeding sustainment at 2 and 6 months.	We had previously provided opportunity to comment on Key Questions and cannot change them at this time, but we did attempt to capture the data on both of these elements as available in the literature.

Commentator & Affiliation	Section	Comment	Response
Peer reviewer #2	Introduction	Introduction: I would be tempted to include a statement about the anxiety and distraction to breastfeeding mothers caused by lack of scientific clarity on this problem. The missed cases of effected infants and the over diagnosis of non-effected infants is a real barrier to sustained breast feeding.	We recognize that this is important, but beyond the scope of the report to speculate.
Peer reviewer #2	Methods	Methods: I appreciate the rigor of two-person review and secondary review by a senior reviewer.	Thank you for your comment.
Peer reviewer #2	Results	Results: It would be helpful to better define the lack of data on CAM techniques. This seems to just be left out.	We have added this to the limitations of the evidence base.
Peer reviewer #2	Results	It would have been helpful to me to have a definition of ”sham surgery,” Page 16 line 12.	We have added this.
Peer reviewer #2	Results	I would hypothesize two potential causes for variation in maternal pain and feeding data verses independent reviewer. One, the parent has significant investment in nonactive procedure on their newborn. Second, most newborns will develop significant ulceration at frenulotomy site. I would imagine this to be quite painful for two to three days. This would explain the immediate improvement with lack of sustainment in maternal pain. The baby cannot develop much suction because it causes pain.	No change needed.
Peer reviewer #3	Discussion / Conclusions	“Implications for Clinical and Policy Decisionmaking” change “or” to “are: in the sentence “…seem to be stronger evidence that harms or minimal to none.”	Thank for your comment; we have made this correction.
Peer reviewer #3	Discussion / Conclusions	Good discussion	Thank you for your comment.
Peer reviewer #3	Executive Summary	In the first sentence, first paragraph: I would define “frenotomy,” “frenulectomy,” and frenuloplasty.”	Thank you for your comment. These terms are defined in the second through fourth sentences within this section.
Peer reviewer #3	Executive Summary	Last sentence in the section: Speech therapy should never be done to stretch the velum. Speech therapy is design to change articulation production. Therefore, I would delete the reference to speech therapy here.	The Key Questions reflect interventions that are done in practice, and we understand that stretching is practiced in some settings, despite a lack of evidence.

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Peer reviewer #3	Executive Summary	There were many separate potential effects of ankyloglossia listed in different sections that were not specifically addressed (i.e., aerophagia, dysphagia, oral hygiene, duration of breast feeding, orthodontic problems, dental caries, failure thrive, etc.) Perhaps list all of these potential sequelae at the beginning in the introduction rather than mentioning it just in different lists throughout the manuscript. Then, I would concentrate on the concerns related to the Key Questions for the rest of the manuscript.	Thank you for your comment. Outcomes sought are listed in Table 3. We reported results or the lack of results on these outcomes in each of the Key Questions.
Peer reviewer #3	Executive Summary	Within Objectives paragraph, remove superfluous "the" and change "anklyloglossia and concomitant lip-tie" to "ankyloglossia with concomitant lip-tie." Within Results paragraph, spell out RCT first time it is used. Perhaps add a definition of frenectomy in parentheses, such as: (procedure in which the lingual frenulum is cut). Within Conclusions paragraph, add summary statement about speech, orthodontic, and self-esteem findings here as well.	Thank you for the suggestions; we have incorporated the changes into the abstract objectives and results and have attempted to summarize key points in the conclusions.
Peer reviewer #3	Executive Summary	In first paragraph add to the definition of ankyloglossia "or an anterior attachment of the lingual frenulum." Also in first paragraph, change "It variably causes reduced tongue mobility" to "tongue tip mobility."	Thank you for the recommendation to expand the definition. While we agree that the tongue tip is most affected, defining the tip is difficult. We have revised the sentence to read "anterior tongue mobility."
Peer reviewer #3	Executive Summary	Key Question 1: Is there really evidence that some people are doing craniosacral therapy, PT, and OT for this?	Our Key Informants report that these practices are occurring. Our intent in listing them there is to be able to identify whether there is any scientific evidence for them (per the report, there is not).

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Peer reviewer #3	Executive Summary	Key Question 2b: Many of these things ("long-term other sequelae") were addressed below.	No change needed.
Peer reviewer #3	Executive Summary	In text describing Analytic Framework A, spell out "PICOTS "with abbreviation.	Thank you for your comment; we have made this addition within the Executive Summary and the Main Report.
Peer reviewer #3	Executive Summary	Figure A, Analytic Framework for Key Questions 1, 4, final outcomes (in the figure) to not match the Key Questions.	We have revised the final outcomes in the analytic framework.
Peer reviewer #3	Executive Summary	Within "Study Population" row: Pierre Robin is a sequence, not a syndrome. It occurs as part of many syndromes.	To ensure clarify we have changed the text to Pierre Robin syndrome/sequence as OMIM and ICD-9 use both terms.
Peer reviewer #3	Executive Summary	Within "Admissible evidence" row: Not sure what a posterior frenulectomy would be versus anterior. You can only make a cut from anterior to posterior. Chiropractic? None of these therapies make common sense. Is there really evidence that this has been done?	We understand that there is little evidence for some of these approaches, but per our key informants, they are in fact being done in practice. It is important to note that and to explain whether or not there is actual evidence. In fact, the American Chiropractic Association has included material about the role of chiropractor in breastfeeding outcomes and ankyloglossia.

Commentator & Affiliation	Section	Comment	Response
Peer reviewer #3	General Comment	There has been a lot of work put into this report. It appears that the reviewers did a very thorough job in searching and analyzing the literature. This is definitely clinically meaningful. Inappropriate frenulectomies are commonly done for speech issues, which are unrelated to ankyloglossia. Unfortunately, a high number of pediatricians, ENTs, and even speech-pathologists believe that when there are speech issues and ankyloglossia, there is a causal relationship. In my long practice, I have found a very rare relationship between the two.	Thank you for your comment.
Peer reviewer #3	General Comment	This is well structured and organized and will help to form practice decisions.	Thank you for your comment.
Peer reviewer #3	Introduction	The introduction is primarily related to early feeding concerns. I would add more information about speech and social concerns, since this was a focus of the Key Questions.	We have added a paragraph about concerns other than feeding, although we note that most research focuses on feeding.
Peer reviewer #3	Results	Results, Key Question 1, Table 7. In note beneath table, perhaps define “G” as well.	We have made sure that all abbreviations are spelled out below the tables for quick reference.
Peer reviewer #3	Results	I like the bullet lists.	Thank you for your comment.
TEP reviewer #1	Discussion / Conclusions	The discussion section is thorough and well organized and I am not aware of any studies which were omitted. The discussion lends itself to generating questions for future research studies.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #1	Executive Summary	The Introduction in the report is well organized and is detailed. I did find, however, that in the Abstract and Executive Summary, there was the suggestion that surgical correction of ankyloglossia was the only option. This was probably due to a need to be concise, because there is no such possible bias in the report itself. But I read these particular sections several times and believe they could be misinterpreted. These areas are: Executive Summary, ES-1, 10 of 274, line 22: Beginning with “Mechanistically,” it seems to me that this sentence and those that follow in this paragraph seem to imply that surgical correction is the only option for infants with ankyloglossia, leading the report to appear biased. The following paragraph opens with “Nonetheless” and further suggests the authors have a preference for surgical correction. Scope of Review, 31 of 274, line 17: The review addresses reported harms, not harms. It is possible, and quite likely, that harms associated with treatment of ankyloglossia have not been systematically reported and it is important that the review not suggest that all harms associated with ankyloglossia have been reviewed.	The paragraph that you reference is about ankyloglossia itself, and not about treatment. In the treatment section that follows there are two distinct sections: one on surgical intervention and one on nonsurgical intervention, in which a number of other treatment approaches are described. We have added a statement about the likelihood of underreporting of harms to the Discussion.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #1	Executive Summary	Clarity and Usability: The manuscript is well structured and organized and the main points can be identified. There are some areas in the Abstract and Executive Summary which were not clear, probably because of a need to be concise, because these issues were explained in the body of the report. The areas which were not clear to me were: Structured Abstract vii (6 of 274), line 30: Future studies could provide additional data to confirm or change the measure of effectiveness.... of frenotomy? Executive Summary: ES-2, KQ4: This question is not clear to me and was not clear throughout the report. Executive Summary: Table A is not clear. The title indicates it contains both inclusion and exclusion criteria but it is not always clear in the table which are inclusion and which are exclusion criteria. Table 4 in the report makes these criteria clear. Executive Summary, ES-6, line 33: It is not clear what is meant by applicability. The conclusions can be used to guide future research questions.	We have changed the title of Table A in the ES to be Inclusion Criteria
TEP reviewer #1	General Comment	This report is of high interest to those involved in treatment of ankyloglossia and has significant clinical meaning in that the review is thorough and that articles reviewed were critiqued against unbiased standards. The population is well-defined and the issues addressed cover an appropriate audience (physicians, lactation consultants, ENTs, dentists, speech-language pathologists, etc.). The Key Questions are appropriate though one question is not clear to me (see clarity).	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #1	Methods	The inclusion and exclusion criteria are justifiable and the search strategies logical. The statistical methods and analysis tools are appropriate; however, I thought that including a summary of the qualifications of the reviewers in the report would strengthen the methods. Also, what was the reliability between reviewers for whether an article should be retained? More importantly, what was the reliability for the quality assessment? How many times did a senior reviewer have to make a final decision?	We have noted reviewer qualifications in the Methods section. Ultimately, a senior reviewer double reviewed all studies to ensure that there was solid agreement. For difficult or complicated studies, the team held discussions at team meetings to ensure consistency.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #1	Results	The amount of detail is generally appropriate. I would include more detail in the section on speech and articulation. In addition, there are some problems with the articles reviewed that should be noted. These issues are: Overview of literature, page 26, 54 of 274, line 15: I believe it may be an overstatement to call the Articulation and Naming Test a validated test of articulation. Data on the validity of this test do not appear available to the public (if validity was conducted). Perhaps the authors obtained a copy of the test and were able to confirm that validity and reliability psychometrics have been conducted. If it is valid, it should be noted that this test was standardized in Hebrew. But including a test possibly standardized in Hebrew with reviews of studies conducted in English is confusing. Also, a problem with the studies of articulation and speech is that when intelligibility was assessed, this measure was assessed perceptually and so has little reliability. Intelligibility varies greatly depending on the familiarity of the listener with the speaker, with the type of production being listened to (words, sentences, etc.), familiarity of the topic, etc. Measures of intelligibility should be made based on published protocols for ways to assess it. Page 26, Line 47: There is no reliability or validity when parents report speech scores. Parents know whether their child received surgery or not. Line 54, page 46: The word “trained” before speech language pathologists suggests a bias that the reader should believe that what the speech pathologist reported was truly accurate. Page 47, line 22: I do not think that it can be said that the assessment tool used was standardized. If it was standardized, it was standardized in Hebrew.	We have deleted the reference to the Articulation and Naming test as validated.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #2	Appendices	Evidence tables are beautifully done. This alone will be extremely helpful to clinicians and researchers.	Thank you for your comment.
TEP reviewer #2	Discussion / Conclusions	Persistent nipple pain can also result from persistence of abnormal sucking movements, which are more entrenched when the infant goes longer without frenotomy. There is evidence that tongue movements during breastfeeding are abnormal apart from latch issues in infants with ankyloglossia (Geddes/Pediatrics). Ingrained motor patterns are difficult to change—think about transitioning from hunt and peck typing to touch typing, something most of us did at some point in our lives.	Thank you for your comment. We did not expand upon this issue specifically because we had no empirical data to do so.
TEP reviewer #2	Discussion / Conclusions	Frenotomy is not a technically difficult procedure compared to transplant surgery, so the concerns about most studies being conducted at tertiary urban institutions is less relevant than for other medical intervention reviews.	Thank you for your comment. We have revised the statement to note that frenotomy procedure itself is not technically difficult and is likely performed similarly across birthing sites.
TEP reviewer #2	Discussion / Conclusions	Otherwise, good summary of limitations and areas that require further research. Well structured, well written. I think the main points will be easily understood and useable for decision making.	Thank you.
TEP reviewer #2	Executive Summary	Table A – frenotomy should be included as a treatment modality with frenulectomy/frenectomy, as most studies actually used frenotomy, despite the language used in the study paper.	Thank you for your comment. This has been corrected.
TEP reviewer #2	Executive Summary	One specific reason that post-frenotomy observer differences were inconsistent and non-significant is that the tools used (LATCH, etc.) are screens and not truly assessments. They do not pick up fine levels of detail in feeding effectiveness. We need better assessment tools, That's one area of research that can be recommended. I'm concerned that maternal report of pain is being discounted as a valid measure. Pain scales are commonly used in medical research.	We agree and have reframed the discussion to make it clear that we do not discount maternal report of pain as a key outcome. Clearly, this outcome could have substantial importance for willingness to continue breastfeeding.

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TEP reviewer #2	General Comment	One issue that is not addressed at all is that of ethics. With breastfeeding at stake, we don't have equipoise. The health importance of breastfeeding to both mother and infant is so compelling that randomization becomes ethically fraught when there is any evidence at all that ankyloglossia reduces breastfeeding duration or effectiveness and frenotomy helps. We need to consider carefully what kind of research design provides good evidence without imperiling breastfeeding. I think that imaging studies like Geddes (Pediatrics 2008) have an important role and should be included more strongly in the evidence base. (Disclosure – my own group's imaging study is being prepared for publication).	Thank you for your comment.
TEP reviewer #2	Introduction	Table 3 – stretching is done as a post-operative therapy to prevent the wound from readhering and requiring revision surgery, not as a primary non-medical therapy for tongue-tie.	Key informants indicated that stretching was being used in some clinical settings as therapy, perhaps inappropriately. Therefore, we intended to allow any available studies of the practice. There were no studies available.
TEP reviewer #2	Introduction	Page 2 – Horizontal to vertical frenuloplasty is also commonly called transverse to vertical frenuloplasty.	We have noted this in our report.
TEP reviewer #2	Introduction	Lactation intervention includes many other strategies, including use of assistive feeding devices at breast and maintenance of milk production.	We preidentified key interventions with our key informants and TEP members. There was an opportunity to comment on Key Questions, but we cannot change the Key Questions at this time.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #2	Introduction	Coryllos criteria is NOT a severity index, it's a classification of presentation, to improve awareness of more subtle tongue-ties. The degree of restriction of tongue mobility is the salient factor for severity, not the location of the frenulum. (I am co-author on that paper, and this was our main point, though the typing system was Dr. Coryllos' alone.) Type 4 are likely to affect swallowing more than sucking, because posterior tongue mobility is crucial for swallowing (see Elad et al. PNAS April 2014). Remember the ”structured assessments” are really screens, meant to allow nonspecialist personnel to triage bf dyads.	Table 2 never refers to the Coryllos criteria as a severity index; it is simply listed as one of the assessments used in ankyloglossia diagnosis, classification and care. Nonetheless, we have changed the title of that table to be: Structured assessments and screening tools used in ankyloglossia literature.
TEP reviewer #2	Results	Tongue tie division is the same procedure as frenotomy.	For this table we used the term used by the study authors because some studies did not provide adequate information to specifically identify the procedure.
TEP reviewer #2	Results	There are no studies of orofunctional myology or oromyofunctional therapy, which are used to retrain tongue movements. This may be because none exist for ankyloglossia yet, but this should be confirmed.	You are correct that no studies of orofunctional myology were identified.
TEP reviewer #2	Results	The percentages used in Griffiths, Hogan, and Berry's studies are percentage of the tongue attached by the frenulum, not lengths of frenula. 100% correllates to a Coryllos type 1, 0% to a Coryllos type 4. Again, it is a presentation description, not a severity index.	We have clarified this in the text.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #2	Results	The spoon feeding item is ambiguous. Solid/pureed foods should not be given to infants under 6 months (and definitely not to infants under 4 months) so it is no wonder that frenotomy did not improve spoon feeding in the one early frenotomy group infant! Tongue thrust exists to prevent ingestion of foods other than milk before 4-6 months of age, and resolved with development. Young infants are able to spoon feed liquids like milk by sucking from the spoon, which is a different process. This is important to differentiate here, or at least note that spoon feeding of anything other than human milk or milk substitutes is inappropriate before 4–6 (and preferably 6) months.	We are confused about this comment as spoon feeding is not described in this section at all. The studies do provide data on bottle feeding.
TEP reviewer #2	Results	Small white patch at base of tongue is healing slough, normal stage in healing of mucosa, is NOT a harm.	We have clarified that this is healing slough. Of note, it is reported in the paper as a component of safety outcomes.
TEP reviewer #3	Discussion/ Conclusion	Discussion/ Conclusion: I feel that the conclusions should be stated in less strong terms that emphasize the low level of confidence in findings, given the potential biases in the reviewed studies, the lack of information about significant and long-term outcomes, and the small sizes of the studies.	We have edited the conclusion.
TEP reviewer #3	Discussion/ Conclusion	Rather than stating "A small body of evidence suggests that frenotomy may be associated with improvements in breastfeeding as reported by mothers, and potentially in nipple pain, but with small, short-term studies, inconsistently conducted, SOE is generally low to insufficient," I would suggest stating that "The low strength of existing evidence does not allow us to draw firm conclusions about the benefits vs risks of frenotomy." In other words, state it in more neutral terms that emphasize the uncertainty and unknowns, rather than stating it as a positive and then adding disclaimers and caveats.	We have revised the conclusion to emphasize further the lack of evidence and low SOE.

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TEP reviewer #3	Discussion/ Conclusion	Emphasize the lack of studies that address the most common clinical question: "In an infant with feeding difficulties thought to be due to a short frenulum, does the use of a frenotomy versus skilled lactation consultation support (or some other conservative management method) result in successful exclusive breast feeding until six months of age?"	We have expanded the limitations of the evidence base to include this concept.
TEP reviewer #3	Executive Summary	Abstract should include summaries of the quantitative results.	Because the quantitative data are sparse and not able to be combined, we elect to leave them out of the abstract.
TEP reviewer #3	General	I would suggest including some statements about the possibility of publication bias, i.e., the possibility that negative trials may not have been published or presented. A funnel plot should be created to assess for this possibility.	Funnel plots are poorly able to properly assess publication bias because of their assumptions regarding the association of study size and outcomes; in the case of this literature base, we would be especially cautious about their use. However, we agree that a statement about potential publication bias should be included and we have added this.
TEP reviewer #3	General	The reports needs to emphasize the lack of information about significant long-term outcomes such as exclusive breast-feeding at six months of age or at one year of age, growth, and other measures of health/morbidity. Most of the outcomes are short-term and subjective ones.	We agree and have added this to the Discussion.
TEP reviewer #3	General	Clarity and Usability: Yes, but the conclusions are not strong enough to make any strong policy or practice recommendations. Given the fact that there is an increasing tendency in clinical practice and in the lactation world to recommend frenotomy, this report should strongly emphasize the unknowns in this field and the weak evidence, so that it is not interpreted as justification for doing more frenotomies. In other words this report should help put the brakes on a runaway trend by pointing out the lack of strong/high-quality evidence.	We believe we have provided a fair assessment of the strengths and weaknesses of the literature.

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TEP reviewer #3	Introduction	Introduction: No comments regarding this section. It is well written.	Thank you for your comment.
TEP reviewer #3	Methods	Methods: Yes to all the above questions	Thank you for your comment.
TEP reviewer #3	Results	Results: Yes to all the above questions. Need to emphasize the general lack of information on several important outcomes such as exclusive breast feeding by six months of age or until one year of age, growth parameters and other measures of health. Most of the outcomes studied are short-term subjective outcomes.	We agree and have done so.
TEP reviewer #4	Discussion / Conclusions	The conclusion should be more clearly stated that the current available evidence supports frenotomy to prevent and treat breastfeeding related problems but the strength of this recommendation is weak due to low strength of the evidence. The conclusion should be more clearly stated that the recommendation is to provide this treatment because it may have the effect desired but the LOE is low.	EPC reports describe the evidence, but do not make recommendations. This will be left to the end user, who will ideally make a guideline and can use the evidence as a part of that process and potentially make stronger statements.
TEP reviewer #4	General	The report is very broad and many of the questions are applicable to a small group of patients and providers. The Key Question that many practitioners have is related to the procedure of frenotomy and its effect on breastfeeding outcomes. The review of this topic is brief and limited by the scant literature deemed to be high in quality.	Thank you for your comment.
TEP reviewer #4	Introduction	Comprehensive and well done.	Thank you for your comment.
TEP reviewer #4	Methods	There are too many Key Questions. It would have been more helpful to focus on the issues of ankyloglossia as it affects breastfeeding/infant feeding.	We appreciate your comment. Key Informants and Technical Experts contributed to defining the questions addressed in this review. We feel that the Key Questions comprehensively address decisional dilemmas faced by clinicians.

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TEP reviewer #4	Results	Recommend focusing more on the studies that were high quality and determining if a meta-analysis would help develop a more definitive recommendation for (or against) frenotomy to prevent breastfeeding problems. Also a focus on short-term problems is more appropriate given that confounding variables affecting more long term breastfeeding success. A forest plot with effect size and group estimate may provide mathematical data combined with the authors' opinion that the strength of the evidence was low to nonexistent would be better advice for practitioners.	Given the dearth of comparative studies on the topic, the report attempts to make use of all the study data available. Several factors (e.g., small number of studies, limited number of comparative studies and the heterogeneity of interventions/outcomes) prevented us from conducting a meta-analysis.
TEP reviewer #5	Discussion / Conclusions	Same here—in fact, more important to discuss how mom's report of improvement alone is very important given common reasons for stopping breastfeeding. Also important to look at Emond study and how the majority of the nonfrentomy group went ahead and got a frenotomy!	Thank you. We agree that maternal report is ultimately a key outcome, and in fact, the more patient-centered outcomes. We report the data and attempt not to suggest that objective outcomes are better in this case.
TEP reviewer #5	General	It is a clinically meaningful report and Key Questions are clear.	Thank you for your comment.
TEP reviewer #5	Methods	No issues here.	Thank you for your comment.
TEP reviewer #5	Overall Clarity and Usability	[The authors] were not able to make many conclusions, but I think it is helpful to guide further research.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #5	Results	One thing here is that it seemed like the benefits were downplayed or called into question because "there was no difference in observer grading." I have a problem with this because a latch can appear very effective from the outside and there can even be evidence of milk transfer with maternal reports of pain and obvious evidence of nipple compression at the end of a feeding. This, therefore would not be an effective latch, or good signaling for the mom, and would not be sustainable unless adjustments were made either to have the baby deeper, change the angle, and/or clip the frenulum if the first two things do not work. I think the fact that an observer cannot "see" the change is not surprising, and that the mother's report of relief of pain and depth is very important. Even though the studies were small, this is an important finding. I would try to restate that one point slightly differently. Did you look at the Elad study 2014? I didn't see that one.	We agree that there is a problem with the observer versus maternal grading, and we have modified language so as not to suggest that observer ratings are necessarily superior to maternal report. The mechanics of breastfeeding as addressed in Elad 2014 are outside the scope of this review. (Elad D, Kozlovsky P, Blum O, Laine AF, Po MJ, Botzer E, Dollberg S, Zelicovich M, Ben Sira L. Biomechanics of milk extraction during breast-feeding. Proc Natl Acad Sci U S A. 2014 Apr 8;111(14):5230-5. doi: 10.1073/pnas.1319798111. Epub 2014 Mar 24. PubMed PMID: 24706845; PubMed Central PMCID: PMC3986202).
TEP reviewer #5	Introduction	I think it is important to mention here that over 80% of mothers initiate breastfeeding, and that very few, 18% make it to 6 months exclusive which is the recommendation. (CDC Breastfeeding Report card 2014), and that nipple pain is in the top three reasons for stopping (IFPS II).	We agree that this is valuable information; however, the Introduction is focused on ankyloglossia and potential treatments and outcomes.
TEP reviewer #6	Discussion / Conclusions	Page 47 line 52: "harms or minimal" I think there is an incorrect word Page 48 line 8 (paragraph 1, sentence 2): This sentence doesn't make sense to me.	Thank for your comments; we have made this correction to the Implication for Clinical and Policy Decisionmaking section.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #6	Discussion / Conclusions	The evidence is well summarized, and it is clear that in most areas the SOE is very low. I would, however, like to debate this for Key Question 1. The fact that 2 blinded RCTs find maternal report of improved effectiveness, I believe shows more than low SOE, especially given the challenges of doing blinded studies for a procedure like this. I think the mom's report is actually more sensitive to changes than the tools we have to use for assessment by a clinician. There is also clearly, a long way to go in expanding overall research in the area of ankyloglosia. I concur that we need better standardization for classifying tongue tie, and we need much better information on the natural history. That said, I also think we need to look at the impact of tongue tie release on the duration of breastfeeding, since that is our ultimate outcome. In discussing Gaps in Research (p 48-49), you discuss durability of outcomes, and mention the need for longer term followup re: effectiveness and pain, but duration of breastfeeding is really the key (though obviously related to pain and effectiveness).	We appreciate that there are 2 blinded RCTs in this area, and that is adequate to categorize the evidence as more than insufficient. However, the studies suffer from many of the concerns we have raised in the report, and they are small, use heterogeneous outcomes, and are inconsistent, so the overall SOE is low, pending future studies. It is important to remember that the low strength of evidence does not mean that the treatment is ineffective; rather the SOE is an indication of our confidence that we know the true effect at this time.
TEP reviewer #6	General Comment	This is a very thorough and comprehensive report. The volume of literature that was considered is impressive. The report is also very well written. That said, there seems to be a tremendous amount of repetition, but I am assuming that is due to the requirements of this type of review. In particular, the Executive Summary was quite lengthy and in depth, but then was repeated in the full report, with little expansion in some sections.	Thank you for your comment. The Executive Summary is, as you mention, a wrap up of the larger Main Report, so some repetition is unavoidable.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #6	General	Well structured and organized, though quite redundant between Executive Summary and main report, and also between sections on some of the Key Questions. Main points are clearly presented. It does provide a large body of information for future researchers to use as a starting point re: literature search and developing research questions and methodology. I hope people using is for policy and practice decisions do read more than the brief conclusions. In my world, the conclusions say that there is not strong research evidence that releasing a tongue tie is helpful, so what I hear clinically is "there is not any evidence that this is helpful, so we will not prescribe it." That is an injustice for many infants, and often dooms their breastfeeding success. I would like our research focus to be on figuring out which infants are more likely to be helped, and by what procedure, done at what time.	We agree that future research should identify subgroups of infants for whom intervention may be most helpful. We also hope that end users will follow through with using this report to develop guidelines, a step that is out of the scope of the EPC program.
TEP reviewer #6	Introduction	Thorough. Well written. Good overview of project.	Thank you for your comment.
TEP reviewer #6	Methods	The inclusion and exclusion criteria are fine, and search strategies are well stated and logical. The volume of literature that was identified and reviewed is very impressive. In regard to strength of evidence, I realize that you are using established tools and following their protocols, but the "bar" seems to be very high. There are not very many questions in the vast expanse of medical practice that will come up with a body of literature with high strength of evidence, even though we are trying to use "evidence based" practice in our clinical work.	No change required.
TEP reviewer #6	Results	The results section is very detailed and the studies that were included are well described. In regard to Key Question 1, I feel like maternal rating of BF effectiveness is not considered to be as valid as rating by an external rater. However, maternal impression of effectiveness may be the most sensitive marker for potential duration of BF (our ultimate goal).	We agree and have revised our writing to make this more clear.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #7	Discussion / Conclusions	Implications of the studies would mean successful breastfeeding. Limitations are described adequately. I am not aware of any studies that were omitted. The report is well structured and organized. Main points are clearly presented.	Thank you for your comment.
TEP reviewer #7	Discussion / Conclusions	Conclusions regarding ankyloglossia's impact on effective breastfeeding seems to be more in the range of moderate SOE rather than a low strength of evidence. The stated rationale for the reason why a low SOE was assigned was that the assessment of improvement was based on maternal report. The AHRQ report also states that these research studies only demonstrated short-term breastfeeding duration. It is important to address both of these points.	The reason for the low SOE is the small number of infants studied, the need for longer term outcomes, and the inconsistency across the literature base. We do not indicate that the low SOE is due to the maternally reported nature of the outcome. As noted above, low SOE does not mean that the intervention does not work, rather that our estimate of its effect is likely to shift with future research.
TEP reviewer #7	General	Regarding the use of maternal reports following frenotomy, tools used in these studies have--in other studies-been validated. These tools also have been shown to have good inter-rater reliability. Here is an example: IBAT Validity study:Schloner, Journal of Human Lactation Inter-rater reliability: Matthew, J Midwifery Thus, a formal validated tool assessed maternal outcome, rather than the mother's informal opinion.	Thank you for this information. We have cited the Matthew study in our description of assessments used in the ankyloglossia literature (table 2).
TEP reviewer #7	General Comment	The report is clinically relevant. The target population and audience is defined. The Key Questions are well defined.	Thank you for your comment.
TEP reviewer #7	Introduction	The introduction is generally satisfactory. The treatment strategy section would benefit from a description of what a lingual frenotomy is (incision of lingual frenulum without need for repair).Clarifying for the reader that frenotomy iand frenulotomy are synonymous terms, would be helpful.	Thank you for your comment. The terminology has been further defined and clarified.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #7	Methods	Regarding inclusion/exclusion criteria, I have a concern about the sentence:“Surgical interventions (simple anterior frenectomy, laser frenulectomy, posterior frenulectomy, Z-plasty repair”.The sentence above uses the word frenectomy (which is surgical removal of lingual frenulum) rather than the word frenotomy (incision of the lingual frenulum without need for repair). A simple frenotomy is the procedure that is most commonly done in babies(not frenectomy). Frenectomies are not as commonly done in infants. The remainder of the methods section (search strategies, diagnostic criteria)is satisfactory.	Thank you for your comment. This has been further clarified. Inclusion criteria now incorporates all surgical/procedures used to describe frenulum division including frenotomy, frenulotomy, frenulectomy, and frenuloplasty. Lack of specificity of terms in the literature and desire to capture all relevant articles requires that the terminology used in inclusion be broad. The term frenulectomy is often used in the literature interchangeably with frenulotomy and therefore it was included in this search.
TEP reviewer #7	Results	The amount of detail presented was satisfactory except for the sentence “Among studies reporting harms, bleeding was most frequently reported. Bleeding was typically described as minor and limited. Few studies described what specific methods they used to collect harms data.” As any oral procedure will produce a small amount of post procedure bleeding, it would also be important to note in the report that all of these articles did not report significant bleeding requiring special intervention The characteristics of the studies was clearly described Key messages were explicit and .applicable No studies were overlooked to my knowledge. No studies should have been excluded.	We have added a note that minor bleeding would be expected with oral surgery.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #7	Results	Regarding the statement that researchers described only short-term positive outcomes, long-term outcomes were actually addressed in both the Buryk and Berry studies. While the duration numbers may seem low at first, when compared to expected overall breastfeeding rates, the outcomes post frenotomy reach expected breastfeeding levels for the overall population .For example,iIn the Buryk study breastfeeding rates at 2, 6, and 12 months were 66%, 44% and 28% respectively. The breastfeeding duration rates in the Berry study at 3 months was 65%. 51%were still breastfeeding at mean of 4.5 months. Post - frenotmy, the mother's breastfeeding durations are on par with breastfeeding levels for the overall population. This represents a success in preventing breastfeeding cessation.	Unfortunately, neither of these studies is able to compare long-term followup by treatment group, in part because most patients go on to request treatment once blinding is removed. So while it is true that longer term numbers are provided, these are non-comparative. It is appropriate to note that it may be very difficult to get long-term comparative data under these circumstances. Nonetheless, we have amended our statement to read" outcome measures were heterogeneous and most were short term."
TEP reviewer #8	Executive Summary	A small body of evidence suggests that frenotomy may be associated with improvements in maternally reported breastfeeding effectiveness and nipple pain among infants with ankyloglossia and feeding difficulties. This is a bit confusing, at least with respect to "nipple pain among infants." Maybe something more like: A small body of evidence suggests that frenotomy performed on infants with ankyloglossia and feeding difficulties may be associated with improvements in maternally reported breastfeeding effectiveness and nipple pain.	Thank you for the suggestion; we have clarified the language.
TEP reviewer #8	General Comment	The results are not surprising as the field is known for poor amounts of data published—hopefully it will prompt thoughtful study and that will improve evidence one way or another. Everything studied is defined well and the questions are appropriate.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
TEP reviewer #8	General Comment	[With regard to overall clarity and usability] It can inform policy minimally given the lack of evidence.	No change needed.
TEP reviewer #8	Introduction	Mechanistically, infants with restrictive ankyloglossia cannot extend their tongues over the lower gum line to form a proper seal and therefore use their jaws to keep the breast in the mouth for breastfeeding I understand some of the words are purposefully nonmedical, but maybe it would sounds better written as: Mechanistically, infants with restrictive ankyloglossia cannot protrude their tongues over the gum line to contact their lips to form a proper latch and therefore use their jaws to keep the maternal nipple in the mouth for breastfeeding.	Thank you for the suggestion; we have made this change.
TEP reviewer #8	Methods	Yes, this all seems very appropriate.	Thank you for your comment.
TEP reviewer #8	Results	Everything looks good. I appreciate the summary of my thesis.	Thank you for your comment and allowing us to cite your research.

Commentator & Affiliation	Section	Comment	Response
Key Informant #1	Executive Summary	A very useful role of this review is to educate clinicians on how ankyloglossia could potentially impact children and their mothers. This information could guide clinicians in taking a history to determine (a) what degree of impairment/problem exists, and (b) how might this influence a decision to intervene or observe. Therefore, I would consider adding a table early on summarizing features that clinicians should ask about in the history of a child with ankyloglossia. These are stated (mostly) in figures A & B (Analytic Frameworks), plus some of the text. Specifically, the questions to ask for neonates/infants are (a) nipple pain, (b) difficult latch, (c) aerophagia, (d) prolonged breast feeding, and (e) weight loss. In older infants and children the issues are (a) articulation disorder, (b) oral hygiene (e.g., cleaning teeth with tongue), and (c) social concerns (licking lips, eating ice cream, kissing).	Thank you for this suggestion. However, the role of the EPC is not to make recommendations and we are limited to summarizing the literature and assessing existing data. We hope that other partner organizations can use this report to develop evidence-based recommendations and materials.
Key Informant #1	Executive Summary	I also would recommend that statements about Harms get greater emphasis in the abstract and manuscript. When evidence of efficacy is weak, or uncertain, the issue of harms and adverse events assumes overriding importance in clinical decision-making. The finding of no significant harms is important, with the main issues being minor, self-limited bleeding or the rare need for reoperation.	While we agree that the issue of harms is extremely important, we are cautious about making stronger statements due to the possibility that there is publication bias at play in when harms are reported and under what circumstances.
Key Informant #1	Executive Summary	Regarding harms, the authors state that "case series" were included, which is appropriate. Harms, however, can also be published as isolated case reports, which are also important and meaningful. Were case reports included?	We identified 14 case reports that included harms. See: ES-8 and page 34 of the Main Report. Appendix G documents these studies and the reported harms.
Key Informant #1	Executive Summary	A potential harm of frenotomy or frenuloplasty is a mucocele of the submandibular or sublingual gland. The authors do not mention this. If none were encountered then I would explicitly state that no mucoceles occurred.	We have added the reference to the one case of mucocele described in the literature.

Commentator & Affiliation	Section	Comment	Response
Key Informant #1	Executive Summary	The discussion of applicability (ES-13) is very good and important. I would mention this in the abstract. Specifically, our confidence in the study findings is further reduced by (a) the lack of details regarding surgical technique, (b) co-interventions that were allowed in the control/sham groups (e.g., lactation consultation, supportive care, bottle-feeding advice), and (c) the diversity of provider settings (surgeon, otolaryngologist, surgeon, unknown).	We have added this to the abstract.
Key Informant #1	Executive summary	The finding that were no studies were identified regarding simultaneous treatment of lip and tongue tie is telling, given that some clinicians market aggressively in this regard. I would emphasize the absence of evidence more in the abstract.	We have added a sentence to the abstract results.
Key Informant #1	General Comment	This is an excellent, methodologically sound systematic review on an important clinical topic with substantive uncertainty regarding management.	Thank you for your comment.
Key Informant #1	General Comment	A main contribution of the review is to highlight the limited evidence to guide clinical decisions, the associated high risk of bias in the available evidence, and the "warts and blemishes" of this body of literature.	Thank you for your comment.
Key informant #1	Results	In Table 6 the description of providers notes that 9 studies had "surgeon" as a provider. Please note that otolaryngologists are considered "surgeons," so the 2 descriptions are not mutually exclusive. Consider changing "surgeons" to "general surgeons" if this is what is meant.	Thank you for the recommendation. We have subdivided the “surgeon” category into “General surgeon” and “Pediatric Surgeon.”
Key informant #2	Discussion / Conclusions	This was a fairly comprehensive review of the literation with a well-articulated information retrieval plan. I am not aware of any key or landmark studies that were omitted. Not only are limitations of the individual studies handled well, but they provide a well stated summary of the limitations to the current body of knowledge on ankyloglossia. I think that they clearly state the implications for practice (but with low strength of evidence.) The also do an excellent job of discussing implications for clinical decision-making and a substantial number of research gaps.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
Key informant #2	General Comment	Clarity and Usability: I think that the authors do an excellent job of creating a well structure and organized report given the relative paucity of well-designed studies. The clearly present findings even with a diversity of Key Questions. I think this will clearly inform practice decisions (page 47, lines 52–54 "Thus, given the mixed evidence, clinicians and families will likely need to make individual decisions about pursuing intervention for ankyloglossia-related feeding and speech impediments." I think that is presents a clear need for future research. I think policy decisions will be more difficult but this report presents the best available evidence.	Thank you for your comment.
Key informant #2	General Comments	This report is clinically meaningful since it is a relatively common problem with interventions not well guided by evidence. The Key Questions are diverse and the authors did an excellent job of pairing target population to the question. The audience for this report is also diverse, so it is likely to be examined by multiple disciplines and specialties.	Thank you for your comment.
Key informant #2	Introduction	Good job of providing an overview of the issues and background of ankyloglossia and various outcomes. An appropriate description is given of the presumed pathophysiology of ankyloglossia and outcomes understudy. Page ES-1 lines 28–32 give the summary of a survey of health professionals and the role they think that ankyloglossia plays in breast feeding difficulties. Lactation consultants were the highest agreement, so it might be nice to have an understanding of any policies or guidance from the International Lactation Consultant Association. The recruitment of Lactation Consultants used that organizations mailing list (Messner AH and Lalakea ML. 2000 (see reference 3 on page ES16).	We did not identify formal guidance or polices from the ILCA.

Commentator & Affiliation	Section	Comment	Response
Key informant #2	Methods	The authors do a good job of developing inclusion and exclusion criteria for the Key Questions. The also use a systematic approach to information retrieval while providing a rationale for decisions about inclusion and exclusion of journal articles. Given the nature of this report, the statistics were largely descriptive which were appropriate.	Thank you for your comment.
Key informant #2	Results	Given the variety study methodologies, focus of the various Key Questions and low quality studies, the authors appropriately summarized data and implications. It helped to be able to refer to the Evidence Tables to view a more graphic summary. Figures, tables and appendices were well defined and labeled, so they could "stand alone" to provide information. Page ES-7, line 12-17 provide a brief description of three studies that used "sham" surgery as the control. It might have been useful to describe how they accomplished sham surgery in a blinded fashion given the type of surgery. While not entirely intuitive, the same approach was used in all three studies.	We have added a brief description.
Key informant #3	Discussion / Conclusions	One area that is reported by some speech-language pathologists is the use of non-surgical techniques (such as stretching) to alleviate the supposed negative effects on speech. So I believe this is a gap as well…the reported but not studied use of nonsurgical techniques for speech improvements.	You are correct that we did not identify any studies of stretching in the literature.
Key informant #3	Discussion / Conclusions	I believe the correct implications were stated based on the data obtained.	Thank you for your comment.
Key informant #3	Executive Summary	Page 6 Line 8 Omit the word "the" before "reviewed"	Thank you for your comment; we have corrected this error.
Key informant #3	Executive Summary	Page 6 Line 40 Awkward wording: "…improvements in articulation but mixed results related to fluent speech." Perhaps better stating: "...improvements in speech articulation but mixed results related to overall speech sound productions." This correct wording was used on Page 72 Line 22. This was mentioned on Page 14 Lines 25/26 in the table.	Thank you for your comment; we have corrected the language to match.

Commentator & Affiliation	Section	Comment	Response
Key informant #3	Executive Summary	Page 10 Line 47 Another nonsurgical technique is not really speech therapy, but rather "stretching" exercises. See comment below under Page 76 Speech and Other Outcomes.	You are correct that we did not identify any studies of stretching in the literature.
Key informant #3	Executive Summary	Page 68 Line 39 "Parental assessment" is probably "parent report" because parent's don't do assessments, professionals do. This also occurred on Page 17 Line 18. Please check for elsewhere, as well.	Both of these pertain to #304 – Walls. Within that article, page 129 indicates "telephone survey.. regarding.. intelligibility of speech to a mother or father… Parents were asked to consider vocabulary development, articulation and impaired sounds when making their judgments regarding speech outcomes"
Key informant #3	Executive Summary	Page 76 Line 24 & 26 "Speech impediment" is a term no longer used. How about "speech production difficulties" instead. This is on Page 23 Line 35 as well. A document search should be done to change all of these.	Thank you for your comment; we have corrected the language.
Key informant #3	General	Page 54 Line 15 (and elsewhere) The preferred naming of the professional is: speech-language pathologists (with a hyphen). It is desirable to NOT call the professional "speech therapist" or "speech pathologist."	Thank you for your comment; we have corrected the naming.
Key informant #3	General Comment	This is very appropriate and attempted to answer the relevant questions around this topic.	Thank you for your comment.
Key informant #3	Introduction	Very thorough and accurate.	Thank you for your comment.
Key informant #3	Methods	Appropriate and well explained.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
Key informant #3	Overall Clarity and Usability	Throughout, when there was a report of "articulation errors" the specific speech sound errors were never reported. This can be an important factor in determining treatment effectiveness. The specific speech sounds that were evaluated and determined to have improved should be noted. The typical speech sound errors with ankyloglossia would not cause intelligibility issues, but rather speech distortions that draw attention to the misproduction, but not influence intelligibility.	We have reported the results as they are available in the papers in the results section for KQ
Key informant #3	Overall Clarity and Usability	Throughout the document: the use of the term "fluent speech" is confusing because "fluent speech" usually means "lack of stuttering." Please us a different way of saying this.	The document reflects the language used in the studies.
Key informant #3	Results	Page 54 Line 5 Instead of saying "speech and articulation concerns," a better way to say this is "…speech articulation concerns." Page 54 Line 14 Same comment as above.	Corrected
Key informant #3	Results	Much detail, as would be expected for such a review.	Thank you for your comment.
Key informant #3	Results	Page 54 Line 31-32 "…age that speech and articulation abnormalities typically present." How about… "…age that speech articulation errors are typically resolved."	We believe that our current text reflects our meaning, which is the age at which speech articulation errors present clinically and decisions are made to address them.
Key informant #3	Results	Page 56 Line 18 (in the table) "…none of the differences was statistically…" should be "none of the differences were statistically…"	The grammar is correct as is. None is singular.
Key informant # 3	Results	Page 54 Line 20 "Articulatory abnormalities" is not a term that is used. "…determine severity of the child's speech misarticulations" would be a better way to state this.	Thank you for your comment; we have corrected the naming.

Commentator & Affiliation	Section	Comment	Response
Key informant #4	Discussion / Conclusions	The conclusions clearly state the decision to treat is based on individual outcome desire, not on any clear-cut evidence of success.	No change needed.
Key informant #4	Discussion / Conclusions	No studies looked at what actually constitutes proper surgical intervention. Just because a tie was released did not mean it was done correctly or deep enough to be effective. This is inferred on page 77, lines 5–7, standards need to be established.	We agree that there is very little description of the surgical process available in the literature and have noted this in our text.
Key informant #4	Discussion / Conclusions	Major findings: no new news Limitations clearly stated refer to the 18 non-English studies that may have been included, and the relatively low number of studies published pg 75 Most of the studies were rated poor pg 71, 55-57 The implications for 4 Key Questions were that few if any good studies have been done and more research is needed. KQ 5 is the only one that has a positive result in that "...harms OR (should be ARE) minimal to none."	Thank you for your comment. We have addressed that typo. [Same as 45 and 68]
Key informant #4	Executive Summary	The Analysis Framework Figures A and B made no sense to me with the boxes and arrows.	This is the standard format for the analytic framework. See: Helfand M, Balshem H. Principles in developing and applying guidance. In: Agency for Healthcare Research and Quality. Methods Reference Guide for Comparative Effectiveness Reviews [posted August 2009]. Rockville, MD. Available at: http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=rr&ProcessID=60.
Key informant #4	General Comment	Target pop. clear, pg.2, lines 13-20 Key questions appropriate pg.11, 22-60, pg 12, 3-4.	Thank you for your comment

Commentator & Affiliation	Section	Comment	Response
Key informant #4	General Comment	Clarity and Usability: The report is well-structured. I would have preferred to see one KQ start to finish, then another section for the next KQ. It was cumbersome the way it is organized.	We appreciate your comment. There are pros and cons to all formatting options. We have chosen to use a standard approach.
Key informant #4	Introduction	Clinically meaningful and very clear that treatment is controversial and results of treatment not 100%.	Thank you for your comment.
Key informant #4	Methods	Inclusion and exclusion criteria are clear and justifiable, pg 38, line 4-49 Criteria for measurement based on Reference #13, pg.78, 47-50.	Thank you for your comment.
Key informant #4	Results	Considering the studies chosen for inclusion, the results are appropriate. The figures, tables and appendices were overwhelming in quantity and very descriptive. The overwhelming number of studies excluded indicates very thorough review, many were easy to exclude simply by the title. I found none that needed to be excluded based on the criteria.	Thank you for your comment.
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	General	As is, your study will be poorly received in the "real world" of clinical application because of its shortcomings. I strongly urge you to include the ultrasound studies in your analysis. Your failure to do so is a huge flaw. As well, the bias you show by including two entities that have yet to be proven, the maxillary lip-tie and the submucosal "posterior" tie, without talking about the lack of data to support the existence, assessment and treatment of both will undermine your credibility as an unbiased report. If you correct these shortcomings, you will have a very strong analysis that will be a welcome addition to the existing literature on the subject. Thank you for your hard work!	The studies that use ultrasound are classified as case series and are de-emphasized due to the study design and strength of evidence. These studies look at tongue mobility and do not have any active comparators. Regarding the comment about lip-tie and posterior tie, we discussed these two entities in depth with the TEP, all of whom had encountered these issues clinically and thus felt they were important to include as part of the review. We identified few studies addressing these entities in the review process, which is noted in the report (see Key Question 4).

Commentator & Affiliation	Section	Comment	Response
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	General Comment	I appreciate the very hard work you put into this study. Some of the results seem to be sound and will inform clinical practice until new research replaces the old and a new analysis performed.	Thank you for your comment.
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	General Comment	Ankyloglossia, by definition, is failure for the tongue blade to differentiate from the tongue tissue mass during embryogenesis. Partial ankyloglossia is what is being addressed in this report. Partial ankyloglossia is commonly referred to as tongue-tie.	No change necessary
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	General Comment	It is curious that the most important question to be posed, (how tongue mobility and motility in infants changes as a result of intervention), is not posed. This mobility question is alluded to but never detailed nor addressed as it pertains to infants and yet there are several studies which looked specifically at tongue mobility and motility changes post frenotomy in infants. One of these studies is cited in your references but I did not see it referred to in the analysis. (Geddes, et al.) There are a total of three ultrasound studies, which look at tongue mobility in tongue-tied infants pre and post frenotomy and compare the tongue mobility against normal controls. Why have these been excluded?	While we appreciate that tongue mobility may be important, it is an intermediate outcome. The comparison of treatment data against normal controls is not the same as comparing treatment versus no treatment in similar populations, which is the focus of comparative effectiveness research. Therefore, the studies that use ultrasound are classified as case series and are de-emphasized for the purpose of this review.

Commentator & Affiliation	Section	Comment	Response
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	General Comment	Lip-tie is referred to both in the posed questions and the analysis and yet lip-tie has not been defined here nor is any literature defining it or supporting its existence cited here. (Because there is none.) The lack of definition and research to support its existence is not addressed anywhere in this report. There are several studies that refer to lip-tie that you cite as if it is a real entity without mentioning that its existence is anecdotal (at best) at this time. Out on the street, there is tremendous controversy about maxillary lip-tie. There is no agreement on definition and no valid, reliable assessment instrument, yet here, the reviewers act as if it is a real entity with evidence behind it. In other words, it is assumed it is a real entity. I suggest that the lack of evidence re: lip-tie be featured in the discussion. Otherwise, the reviewers show a bias.	The definition of lip-tie is unclear at this time, and some clinicians question its existence. Nonetheless, given increasing discussion of this clinical entity, key informants supported including it in this report. No change is needed.
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	General Comment	Some sections are beautifully written and others seem weak by comparison. I am particularly remembering the middle paragraphs of the introduction that seem a bit unclear with poorly supported assertions.	We have edited the report throughout to improve coherence.

Commentator & Affiliation	Section	Comment	Response
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	Introduction	As to the HATLFF, as its author I must correct your mis-statements made about the scoring on page 3. You cite two articles as the references for the quotes made in regard to correct scoring. You fail to cite the original reference, my thesis, by the name of *The Assessment Tool for Lingual Frenulum Function: Use in a Lactation Consultant Private Practice.* In it you will find the explanation for correct scoring. The Emond article did not use the original HATLFF for their study, and when I went to Bristol to consult with them, I found them scoring the instrument entirely incorrectly. Even with some training they persisted in misquoting me. A score of 6–12 does not indicate mild to moderate tongue-tie. They decided to call it mild to moderate with that function score. <6 does not indicate severe tongue-tie. I do not approve of this and they did not have my permission to make these assertions. This is misrepresentation of my original work. Tongue-tie is tongue-tie. The frenotomy decision rule is <11 on function AND <8 on appearance. My thesis is the first prospective study using the HATLFF looking at tongue function pre and post frenotomy in infants. The HATLFF is valid, reliable, sensitive and specific. It is the only screening assessment performed on infants that meets these research criteria. I strongly suggest you read the original study to use in your description of the scoring. I have attached a copy of the HATLFF chart that contains the scoring segment. You may obtain my thesis at www.AlisonHazelbaker.com via download. I am, frankly, quite surprised it did not show up in your literature search.	We have corrected the table. Your thesis did not appear because it is not an indexed publication in the databases used for this review and was not identified through a gray literature search. Our search was for intervention studies that would fall within the scope of the review, so it would be unlikely that this thesis would meet criteria for inclusion. We note that obtaining your thesis requires paying for it on your Web site.

Commentator & Affiliation	Section	Comment	Response
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	Introduction	Table 2 lists the Coryllos criteria as the only classification schema in your reviewed studies. Are you sure? There are multiple classification schemata cited in the English-language literature. I would double check this and include any other schemata appearing in the included literature otherwise you may appear to be biased for this schema and against the others. By the way, none of the classification schemata have been tested for validity and reliability. Perhaps you should make a statement in regard to this?	The report reflects what was used in the studies that were included.
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	Introduction	In paragraph one of the introduction, sentence two: "While it can be associated with other craniofacial abnormalities, it is most often an isolated anomaly." You cite one study to support this statement. Weak evidence at best. We actually have very little literature to support such a statement. Anecdotally, we find high arched palate and other gum and oral anomalies often accompanying tongue-tie. These have yet to be quantified and studied. I suggest that this sentence either be stricken or clarified to reflect the paltry data on this subject. Like: "it may sometimes occur as an isolated anomaly."	We have revised that sentence.

Commentator & Affiliation	Section	Comment	Response
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	Introduction	Your assertions about the difficulty of diagnosing posterior tie are unfounded. Again you cite one study in paragraph two of the introduction. The HATLFF has been diagnosing posterior ties since it became available. (1993). Now, if what you mean to say is that "submucosal" tie is hard to diagnose then you would be correct, anecdotally. *There is not a single study that has confirmed the existence of submucosal tie*. It is merely asserted that such an entity exists. Anecdotally, submucosal ties disappear when these babies receive bodywork. This anecdotal data, from all over the world, indicates that there are other forms of tongue restrictions that do not fall into the partial ankyloglossia category. And yet, you seem to presume it does exist without discussing it in your analysis as a mere assertion. That means that the incidence statistics for "posterior tie" (read submucosal tie) cannot possibly be accurate. Data from Australia shows that true posterior ties (as diagnosed using the HATLFF) occur more often in boys, just as do anterior ties. This data is as yet unpublished but is being written up. To avoid bias, I think you need to address the lack of evidence for submucosal tie in your analysis.	We do not use anecdotal information in our evidence review, as this does not meet our inclusion criteria.

Commentator & Affiliation	Section	Comment	Response
Public reviewer #1 (Alison K. Hazelbaker, PhD, IBCLC, FILCA, CST, RCST)	Methods	It is unclear as to the validity and reliability of the Cochrane Risk of Bias Tool and the other tools you used for your analysis. Please add validity and reliability statements in the pertinent paragraphs where you explain your process.	The Cochrane Risk of Bias tool is the predominant tool in the systematic review field for assessing RCTs. It has been used extensively and is validated. It is furthermore an accepted approach of the EPC program, whose methods are freely available online: Viswanathan M, Ansari MT, Berkman ND, Chang S, Hartling L, McPheeters LM, Santaguida PL, Shamliyan T, Singh K, Tsertsvadze A, Treadwell JR. Assessing the Risk of Bias of Individual Studies in Systematic Reviews of Health Care Interventions. Agency for Healthcare Research and Quality Methods Guide for Comparative Effectiveness Reviews. March 2012. AHRQ Publication No. 12-EHC047-EF. Available at: www.effectivehealthcare.ahrq.gov.
Public reviewer #2: American Academy of Pediatrics Section on Breastfeeding	Discussion	The conclusion should be more clearly stated that the current available evidence supports frenotomy to prevent and treat breastfeeding related problems but the strength of this recommendation is weak due to low strength of the evidence. As above, the conclusion should be more clearly stated that the recommendation is to provide this treatment because it may have the effect desired but the LOE is low.	The role of the EPC report is to describe the evidence, rather than to make statements in support of clinical practice. We hope that our report will be used by organizations to develop evidence-based clinical guidelines.
Public reviewer #2: American Academy of Pediatrics Section on Breastfeeding	General Comment	The report is very broad and many of the questions are applicable to a small group of patients and providers. The Key Question that many practitioners have is related to the procedure of frenotomy and its effect on breastfeeding outcomes. The review of this topic is brief and limited by the scant literature deemed to be high in quality.	Thank you for your comment.

Commentator & Affiliation	Section	Comment	Response
Public reviewer #2: American Academy of Pediatrics Section on Breastfeeding	Introduction	A small body of evidence suggests that frenotomy may be associated with improvements in breastfeeding as reported by mothers, and potentially in nipple pain, but with small studies, inconsistently conducted, strength of the evidence is generally low to insufficient. Research is lacking on nonsurgical interventions as well as on outcomes other than breastfeeding, particularly speech and dental outcomes. Harms are minimal and rare; the most commonly reported harm is self-limited bleeding. Future research is needed on a range of issues, including prevalence and incidence of 2 ankyloglossia and problems with the condition. The field is currently challenged by a lack of standardized approaches to assessing and studying the problems of infants with ankyloglossia. Better assessment of infants with possible ankyloglossia diagnosed early and consistently (because these infants may have the biggest effect of frenotomy) and randomized and blinded for a study with better measurements of maternal pain and breastfeeding outcomes (such as milk supply, milk transfer and weight gain) is needed. If the studies are done with infants in the first week of life, there would be time for several days of observation in a control group treated without frenotomy by providers with expertise in breastfeeding giving non-surgical treatment and the same outcome evaluation. These infants without improvement could then be crossed over if needed. The studies need to be large enough to see a short-term effect on pain and breastfeeding duration and exclusivity. There are so many factors affecting long-term outcomes of breastfeeding that expecting frenotomy to significantly increase this may not be realistic.	Thank you for your comment. No change is needed.
Public reviewer #2: American Academy of Pediatrics Section on Breastfeeding	Methods	There are too many Key Questions. It would have been more helpful to focus on the issues of ankyloglossia as it affects breastfeeding/infant feeding.	These Key Questions were developed with input from key informants and also posted for public comment.

Commentator & Affiliation	Section	Comment	Response
Public reviewer #2: American Academy of Pediatrics Section on Breastfeeding	Results	Recommend focusing more on the studies that were high quality and determining if a meta-analysis would help develop a more definitive recommendation for (or against) frenotomy to prevent breastfeeding problems. Also a focus on short-term problems is more appropriate given that confounding variables affect more long-term breastfeeding success. A forest plot with effect size and group estimate may provide mathematical data combined with the authors' opinion that the strength of the evidence was low to nonexistent would be better advice for practitioners.	We determined that a meta-analysis would not be appropriate given the heterogeneity of the studies available for review. We provide the data available on all outcomes, but focus on short-term outcomes as these are most commonly available.
Public reviewer #2: American Academy of Pediatrics Section on Breastfeeding	Results	Add forest plot.	We did not conduct a meta-analysis and therefore did not produce a forest plot.
Public reviewer #3: American Academy of Pediatrics Section on Otolaryngology – Head and Neck Surgery	General Comment	The AHRQ draft astutely notes that there exists very little meaningful literature to demonstrate a clear benefit of frenotomy in the neonate or young infant with breast feeding difficulties. While most reports are testimonials and case series, there are placebo controlled studies with sham surgeries that do show scientifically validated reduction or elimination of maternal breast pain during feeds. Additionally, in the hands of an experienced clinician, office-based frenotomy may be performed safely with minimal risk of bleeding or disruption of the submandibular papillae in the floor of the mouth. There is no demonstrated benefit using an office-based laser to perform the procedure for precision of frenulum incision, reduced bleeding or enhanced healing in infants.	Thank you for your comment. No change is needed.

Commentator & Affiliation	Section	Comment	Response
Public reviewer #3: American Academy of Pediatrics Section on Otolaryngology – Head and Neck Surgery	General Comment	The issue of "posterior ankyloglossia" specifically needs to be addressed. There are no clear criteria on physical examination to indicate which patients will benefit from frenotomy and which patients will continue to have feeding difficulties such as improper latching or maternal breast pain. A thick band to one observer may be viewed as normal to another. Clinicians should avoid using the term "submucosal posterior ankyloglossia" since this connotes a normal appearing tongue and frenulum with normal mobility, yet some ongoing but poorly appreciated feeding difficulty. Therefore, the report should offer no definitive guideline without adequate studies to examine this entity. Collectively, the Section on Breastfeeding, the Section on Otolaryngology – HNS, and the lactation consultant community should explore this further to develop a reasonable guideline for parents. The issue of lip-tie or maxillary labial frenum and its potential relationship to any feeding difficulty is poorly understood. Currently, there exists no literature to support release of the maxillary frenum as a means to improve breastfeeding. Infants with feeding difficulties should undergo a medical evaluation for potential causes and treatment options, as ankyloglossia is only one possible cause.	Thank you for your comment. No change is needed.